CORRESPONDENCE

II

REMARKS ON "BIVATOL" AND "BILIPOSOL"

DEAR SIRS,

"Bivatol" and "biliposol" are both prepared and marketed in this country by the Anglo-French Drug Co. Ltd., and its associated Company, Modern Pharmacals Ltd., 11 and 12 Guilford Street, London, W.C.1. "Bivatol" is the trade name given to basic bismuth α-carbethoxy-β-methylnonoate, which forms a limpid oily solution containing 0·035 gm. of metallic bismuth per cubic centimetre.

"Biliposol," on the other hand, is the trade name given to a solution of camphocarbonate of bismuth in ether-purified olive oil, containing 0·04 gm. of metallic bismuth per cubic centimetre.

The chief recommendation for the use of solutions of bismuth salts in oils is that they tend to avoid the rapid and possibly toxic effects of the water-soluble salts on the one hand and the formation of depôts of the metal or insoluble salts on the other. It is only recently that much has been learnt in regard to the solubility of bismuth salts in oil.

Picon (1928 and 1929) states that normal bismuth salts $(R . CO_2)_3Bi$ of higher fatty acids are soluble in non-oxygenated organic solvents such as benzene and slightly soluble in oils, though in water or methyl alcohol they readily dissociate, giving insoluble basic salts, $R . CO_2BiO$. Bismuth salts of acids containing unsaturated nuclei (*e.g.*, benzoic) are insoluble in oils or organic solvents, but the normal bismuth salts of acids containing saturated homocyclic nuclei are oil-soluble, *e.g.*, bismuth camphocarbonate $(C_{11}H_{15}O_3)Bi$ is soluble in oils (to the extent of 33 per cent.) and all organic solvents.

Easson and Pyman (1933) believe that it is better to administer the bismuth in the form of a true basic salt $R . CO_2BiO$ rather than as a normal salt $(R . CO_2)_3Bi$ in order to reduce as far as possible the ratio of extraneous matter to bismuth.

Unfortunately there is even less information on the oil-solubility of basic bismuth salts than on that of normal salts. Easson and Pyman (1933) were unable to confirm the observation of Mignot (1929) that Azam's basic bismuth β-phenyl-α-methylpropionate is oil soluble, as their preparations of the basic salt were only very slightly soluble.

Easson and Pyman were also unable to prepare a true basic bismuth camphocarbonate of the formula $R . CO_2BiO$. Two commercial preparations of bismuth camphocarbonate, namely "Sol-bi" (*Quart. J Pharm.*, 1932, **5,** 160) and "Bismocymol" (*J. Am. Med. Ass.*, 1932, **98,** 1158), are said to contain a salt intermediate between the normal and basic salt.

In regard to the solubility in oil of "bivatol," it is claimed by the Laboratoire français de Chimiotherapie and Girard (B.P., 356, 550 of 1931) that bismuth salts of malonic acid esters of the general formula $R . CH(CO_2R^1) . CO_2Bi(OH)_2$ are soluble in oil where R contains at least 7 atoms of carbon and has one or more branch chains. The ready solubility in oil of basic bismuth α-carbethoxy-β-methylnonoate, "bivatol," was confirmed by Easson and Pyman (1933), who also found that if a saturated homocyclic residue was introduced into the molecule of a half-malonic ester successful results were obtained, as basic bismuth α-carbethoxy*cyclo*hexylacetate (stabismol) was readily

soluble in oils as were the corresponding carbomethoxy, carbo-*n*-propoxy- and carbo-*n*-butoxy compounds (Boots Pure Drug Co. Ltd., Pyman and Fasson, B.P., 381, 362 of 1932).

There are thus a number of basic bismuth salts readily soluble in oils suitable for inoculation in the treatment of syphilis.

Yours faithfully,

G. M. FINDLAY.

THE EDITORS "THE BRITISH JOURNAL OF VENEREAL DISEASES."

The Administration of Arsenic—regularity of dosage.

DEAR SIRS,

Re Col. Harrison's letter in the July number of the "B.J.V.D."

The point that I intended to make was that in the course given at the Seamen's Dispensary regularity is essential. It has been proved again and again that total dosage given in a course is of no avail if the course has been broken, and that a dose of 0·75 gm. will not make up for the absence of a 0·3 gm. dose due four days previously. From Col. Harrison's articles I had not gathered that he regarded regularity of dosage as an essential. In fact his article on the treatment of seamen published in "THE BRITISH JOURNAL OF VENEREAL DISEASES," January, 1930, would appear to refute this idea.

I am,

Yours, etc.,

ERNEST E. PREBBLE.